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=> File .Biotech
=> s (Factor VIII or FVIII or Factor 8)
L1      58450 (FACTOR VIII OR FVIII OR FACTOR 8)

=> s l1 and (blood(l)coagul?)
L2      13760 L1 AND (BLOOD(L) COAGUL?)

=> s l2 and (Willebrand factor or vWF)
L3      3104 L2 AND (WILLEBRAND FACTOR OR VWF)

=> s l3 and (prepar? or purif? or recover? or immunopurif? or affinity purif?)
L4      1236 L3 AND (PREPAR? OR PURIF? OR RECOVER? OR IMMUNOPURIF? OR AFFINI
        TY PURIF?)

=> s l4 and (filter? or filtr?)
L5      570 L4 AND (FILTER? OR FILTR?)

=> s l5 and (pore or porus)
L6      260 L5 AND (PORE OR PORUS)

=> s l5 and (pore or porous)
L7      293 L5 AND (PORE OR POROUS)

=> s l7 and(ultrafiltr? or diafiltr? or nanofiltr?)
L8      105 L7 AND(ULTRAFILTR? OR DIAFILTR? OR NANOFILTR?)

=> s l8 and (Ca or Ca2 or calcium or CaCl2 or Calcium Chloride)
L9      102 L8 AND (CA OR CA2 OR CALCIUM OR CACL2 OR CALCIUM CHLORIDE)

=> s l9 and (dissociat? or ion exchange chromatograph?)
L10     84 L9 AND (DISSOCIAT? OR ION EXCHANGE CHROMATOGRAPH?)

=> s l10 and (cryoprecipitat? or haparin precipitat?)
L11     1 L10 AND (CRYOPRECIPITAT? OR HAPARIN PRECIPITAT?)

=> d l11 bib ab

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L11  ANSWER 1 OF 1  USPATFULL on STN
AN   85:4746  USPATFULL
TI   Preparation of highly purified human antihemophilic
      factor
IN   Chavin, Stephen I., Rochester, NY, United States
      Fay, Philip J., Rochester, NY, United States
PA   University of Rochester, Rochester, NY, United States (U.S. corporation)
PI   US 4495175          19850122
AI   US 1982-405456      19820805 (6)
DT   Utility
FS   Granted
EXNAM Primary Examiner: Rosen, Sam
LREP  Aston, David J., Leitereg, Theodore J.
CLMN  Number of Claims: 10
ECL   Exemplary Claim: 1,7
DRWN  5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 512
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB   Highly purified, biologically active Human Antihemophilic
      Factor (AHF) preparations are prepared having
      specific activities of about 4000-8000 units per milligram of AHF. In
      the method of preparation an AHF concentrate, prepared
      by fractionation of plasma to partially remove fibrinogen, fibronectin
      and other plasma components is subjected to a separation on the basis of
      Stokes' radius to separate AHF from the bulk of remaining proteins in
      the AHF concentrate. The pooled fractions containing AHF activity are
      concentrated by precipitation with ammonium sulfate, sodium sulfate,
      etc., by diafiltration, by PEG addition, or the like. The

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concentrate, is solubilized or equilibrated in an aqueous medium and treated to change the effective Stokes' radius of the AHF to an apparently low value and then subjected to a separation from the concentrate. The AHF pool from above is treated to remove cations by dialysis against an appropriate buffer of lower ionic strength and chromatographed on an anion-exchange medium. The AHF fraction from the above chromatography, is a highly **purified AHF preparation**.

=> s l10 and (solvent or detergent)

L12 81 L10 AND (SOLVENT OR DETERGENT)

=> s l12 and (CHTOUROU A? or NOGRE M? or PORTE P?)/au

L13 0 L12 AND (CHTOUROU A? OR NOGRE M? OR PORTE P?)/AU

=> s CHTOUROU, A?/au

L14 25 CHTOUROU, A?/AU

=> s l12 and l14

L15 0 L12 AND L14

=> s l14 and (Factor VIII or FVIII solution)

L16 6 L14 AND (FACTOR VIII OR FVIII SOLUTION)

=> s l12 and l16

L17 0 L12 AND L16

=> s NOGRE, M?/au

L18 2 NOGRE, M?/AU

=> d l18 1-2 bib ab

L18 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:404998 CAPLUS

DN 131:49441

TI Method for preparing virus-free factor VIII solution by filtration

IN Chtourou, Abdessatar; **Nogre, Michel**; Porte, Pierre

PA Laboratoire Francais du Fractionnement et des Biotechnologies, Fr.

SO PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	WO 9931138	A1	19990624	WO 1998-FR2715	19981214
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2772381	A1	19990618	FR 1997-15888	19971215
	FR 2772381	B1	20010608		
	CA 2314610	AA	19990624	CA 1998-2314610	19981214
	AU 9915681	A1	19990705	AU 1999-15681	19981214
	AU 752271	B2	20020912		
	EP 1037923	A1	20000927	EP 1998-959975	19981214
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002508396	T2	20020319	JP 2000-539061	19981214
PRAI	FR 1997-15888	A	19971215		
	WO 1998-FR2715	W	19981214		

AB The invention concerns a method for preparing by filtration a factor VIII solution which is essentially free of virus and high mol. weight vWF. The method comprises preparing a solution containing high or very high purity factor

VIII essentially free of high mol. weight VIII-vWf complexes and filtering the solution with a hydrophilic filter with porosity as low as 15 nm, such as Planova 15N (Asahi Chemical). Chaotropic ions, such as provided by CaCl₂, may be used to effectuate the dissociation. The type of divalent ion and its concentration affected the yield. 0.35M CaCl₂ is preferred. Both filtration pressure and temperature were found to affect the yield: pressure less than

that

recommended by the manufacturer is used and the temperature is advantageously about 35°.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 2 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

AN 1999-360082 [31] WPIDS

DNC C1999-106780

TI Removing viruses from factor VIII solution - by filtration on nanoporous hydrophilic filter.

DC B04

IN CHTOUROU, A; **NOGRE, M**; PORTE, P; CHTOUROU, A S

PA (FRFR-N) LAB FR DU FRACTIONNEMENT & BIOTECHNOLOGI

CYC 23

PI FR 2772381 A1 19990618 (199931)* 24

WO 9931138 A1 19990624 (199932) FR

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU CA JP US

AU 9915681 A 19990705 (199948)

EP 1037923 A1 20000927 (200048) FR

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

JP 2002508396 W 20020319 (200222) 27

AU 752271 B 20020912 (200264)

ADT FR 2772381 A1 FR 1997-15888 19971215; WO 9931138 A1 WO 1998-FR2715

19981214; AU 9915681 A AU 1999-15681 19981214; EP 1037923 A1 EP

1998-959975 19981214, WO 1998-FR2715 19981214; JP 2002508396 W WO

1998-FR2715 19981214, JP 2000-539061 19981214; AU 752271 B AU 1999-15681

19981214

FDT AU 9915681 A Based on WO 9931138; EP 1037923 A1 Based on WO 9931138; JP 2002508396 W Based on WO 9931138; AU 752271 B Previous Publ. AU 9915681, Based on WO 9931138

PRAI FR 1997-15888 19971215

AB FR 2772381 A UPAB: 20021105

Process for preparing a virus-safened solution of factor VIII (FVIII) containing no high-molecular-weight von Willebrand factor (vWF) comprises (a) preparing a high-purity FVIII solution containing or not containing high-molecular-weight vWF-FVIII complexes, (b) dissociating any high-molecular-weight vWF-FVIII complexes in the solution, and (c) filtering the solution on a hydrophilic filter having a pore size as low as 15 nm.

USE - for treating haemophilia A.

ADVANTAGE - The process removes both high-molecular-weight vWF and viruses, including small viruses such as parvovirus B19.

Dwg.0/1

=> s PORTE, P?/au

L19 126 PORTE, P?/AU

=> s l12 and l19

L20 0 L12 AND L19

=> s l19 and (Factor VIII or FVIII solution)

L21 10 L19 AND (FACTOR VIII OR FVIII SOLUTION)

=> s l16 or l18 or l21 and (filtr? or filter? factor VIII or FVIII)

L22 6 L16 OR L18 OR L21 AND (FILTR? OR FILTER? FACTOR VIII OR FVIII
)

=> Dup rem L22
PROCESSING COMPLETED FOR L22
L23 4 DUP REM L22 (2 DUPLICATES REMOVED)

=> d l23 1-4 bib ab

L23 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:404998 CAPLUS
DN 131:49441
TI Method for preparing virus-free **factor VIII** solution
by **filtration**
IN **Chtourou, Abdessatar; Nogre, Michel; Porte,**
Pierre
PA Laboratoire Francais du Fractionnement et des Biotechnologies, Fr.
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9931138	A1	19990624	WO 1998-FR2715	19981214
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2772381	A1	19990618	FR 1997-15888	19971215
	FR 2772381	B1	20010608		
	CA 2314610	AA	19990624	CA 1998-2314610	19981214
	AU 9915681	A1	19990705	AU 1999-15681	19981214
	AU 752271	B2	20020912		
	EP 1037923	A1	20000927	EP 1998-959975	19981214
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002508396	T2	20020319	JP 2000-539061	19981214
PRAI	FR 1997-15888	A	19971215		
	WO 1998-FR2715	W	19981214		

AB The invention concerns a method for preparing by **filtration** a **factor VIII** solution which is essentially free of virus and high mol. weight vWF. The method comprises preparing a solution containing high or very high purity **factor VIII** essentially free of high mol. weight VIII-vWf complexes and filtering the solution with a hydrophilic filter with porosity as low as 15 nm, such as Planova 15N (Asahi Chemical). Chaotropic ions, such as provided by CaCl₂, may be used to effectuate the dissociation. The type of divalent ion and its concentration affected the yield.
0.35M CaCl₂ is preferred. Both **filtration** pressure and temperature were found to affect the yield: pressure less than that recommended by the manufacturer is used and the temperature is advantageously about 35°.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 4 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-360082 [31] WPIDS
DNC C1999-106780
TI Removing viruses from **factor VIII** solution - by **filtration** on nanoporous hydrophilic filter.
DC B04
IN **CHTOUROU, A; NOGRE, M; PORTE, P;**
CHTOUROU, A S
PA (FRFR-N) LAB FR DU FRACTIONNEMENT & BIOTECHNOLOGI
CYC 23
PI FR 2772381 A1 19990618 (199931)* 24
WO 9931138 A1 19990624 (199932) FR

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU CA JP US

AU 9915681 A 19990705 (199948)

EP 1037923 A1 20000927 (200048) FR

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

JP 2002508396 W 20020319 (200222) 27

AU 752271 B 20020912 (200264)

ADT FR 2772381 A1 FR 1997-15888 19971215; WO 9931138 A1 WO 1998-FR2715

19981214; AU 9915681 A AU 1999-15681 19981214; EP 1037923 A1 EP

1998-959975 19981214, WO 1998-FR2715 19981214; JP 2002508396 W WO

1998-FR2715 19981214, JP 2000-539061 19981214; AU 752271 B AU 1999-15681 19981214

FDT AU 9915681 A Based on WO 9931138; EP 1037923 A1 Based on WO 9931138; JP 2002508396 W Based on WO 9931138; AU 752271 B Previous Publ. AU 9915681, Based on WO 9931138

PRAI FR 1997-15888 19971215

AB FR 2772381 A UPAB: 20021105

Process for preparing a virus-safened solution of **factor**

VIII (**FVIII**) containing no high-molecular-weight von

Willebrand factor (vWF) comprises (a) preparing a high-purity

FVIII solution containing or not containing

high-molecular-weight vWF-**FVIII** complexes, (b) dissociating any

high-molecular-weight vWF-**FVIII** complexes in the solution, and

(c) filtering the solution on a hydrophilic filter having a pore size as low as 15 nm.

USE - for treating haemophilia A.

ADVANTAGE - The process removes both high-molecular-weight vWF and viruses, including small viruses such as parvovirus B19.

Dwg.0/1

L23 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

AN 1992:67159 CAPLUS

DN 116:67159

TI Method for preparing high-purity **factor VIII** including a rapid immunoadsorption step

IN **Chtourou, Abdessatar**

PA Fondation Nationale de Transfusion Sanguine, Fr.

SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9118017	A1	19911128	WO 1991-FR400	19910517

W: CA, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE

FR 2662166	A1	19911122	FR 1990-6252	19900518
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PRAI FR 1990-6252 19900518

AB A method for preparing high-purity **Factor VIII** from a complex aqueous mixture containing von Willebrand Factor-complexed **Factor VIII** includes immunoadsorption on an anti-**Factor VIII** monoclonal antibody. The method is characterized in that (a) a sufficient quantity of divalent ions is added to the complex aqueous mixture to ensure the dissociation of the **Factor VIII**/von Willebrand Factor complex; (b) the mixture containing **Factor VIII** is contacted with an immunoadsorbent consisting of an anti-**Factor VIII** monoclonal antibody which is immobilized on a rigid support by a covalent bond, the monoclonal antibody being so selected that it is directed against the light chain of the **Factor VIII** and can both inhibit the coagulative activity of the **Factor VIII**:C and bond the **Factor VIII** through strong hydrophobic interactions; and (c) the immunoadsorbent **Factor VIII** solution is eluted. **Factor VIII** was purified from cryoprecipitated blood plasma by treatment with

CaCl₂ and viral inactivation solution, immunoadsorption on monoclonal antibody 463A8-Sepharose S1000 gel, elution with buffer containing Tween 80, and ion exchange chromatog. on Q Sepharose FF. The 463A8 antibody was prepared by standard hybridoma methods.

L23 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

AN 1991:614824 CAPLUS

DN 115:214824

TI Concentrated solutions of blood coagulation **factor VIII**

IN **Chtourou, Abdessatar**

PA Fondation Nationale de Transfusion Sanguine, Fr.

SO PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9113625	A1	19910919	WO 1991-FR211	19910315
	W: US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	FR 2659557	A1	19910920	FR 1990-3328	19900315
	FR 2665364	A2	19920207	FR 1990-9828	19900801
	EP 472711	A1	19920304	EP 1991-906628	19910315
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
PRAI	FR 1990-3328		19900315		
	FR 1990-9828		19900801		
	WO 1991-FR211		19910315		

AB Concentrate **factor VIII** solns. of intermediate purity are prepared from cryoppts. by controlled double precipitation, in order to remove the

undesired proteins in 2 stages. Human blood plasma cryoppt. (20 g) was dissolved in 4 times its volume of 20 mM tris-HCl buffer (pH 7). The pH was adjusted to 7.1 (0.5N HAcO), followed by treatment with 24 units heparin/mL, centrifugation, treatment of the supernatant with Al(OH)₃ (110 g/l kg cryoppt.), pH adjustment to 6 with 0.5N HAcO, and centrifugation, to give the **factor VIII** concentrate

=> s 112 and 123

L24 0 L12 AND L23

=> s 123 and (Ca or Ca₂ or Calcium or CaCl₂ or Calcium Chloride)

L25 2 L23 AND (CA OR CA₂ OR CALCIUM OR CaCl₂ OR CALCIUM CHLORIDE)

---Logging off of STN---

ENTER ANSWER NUMBER OR RANGE (1):END

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Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 14:46:59 ON 22 JUN 2004